Accuracy of Physical Examination, Ultrasonography, and Mammography in Predicting Residual Pathologic Tumor Size in Patients Treated With Neoadjuvant Chemotherapy

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Objective: To assess the accuracy of physical examination, ultrasonography, and mammography in predicting residual size of breast tumors following neoadjuvant chemotherapy.

Background: Neoadjuvant chemotherapy is an accepted part of the management of stage II and III breast cancer. Accurate prediction of residual pathologic tumor size after neoadjuvant chemotherapy is critical in guiding surgical therapy. Although physical examination, ultrasonography, and mammography have all been used to predict residual tumor size, there have been conflicting reports about the accuracy of these methods in the neoadjuvant setting.

Methods: We reviewed the records of 189 patients who participated in 1 of 2 protocols using doxorubicin-containing neoadjuvant chemotherapy, and who had assessment by physical examination, ultrasonography, and/or mammography no more than 60 days before their surgical resection. Size correlations were performed using Spearman rho analysis. Clinical and pathologic measurements were also compared categorically using the weighted kappa statistic.

Results: Size estimates by physical examination, ultrasonography, and mammography were only moderately correlated with residual pathologic tumor size after neoadjuvant chemotherapy (correlation coefficients: 0.42, 0.42, and 0.41, respectively), with an accuracy of ±1 cm in 66% of patients by physical examination, 75% by ultrasonography, and 70% by mammography. Kappa values (0.24–0.35) indicated poor agreement between clinical and pathologic measurements.

Conclusion: Physical examination, ultrasonography, and mammography were only moderately useful for predicting residual pathologic tumor size after neoadjuvant chemotherapy.

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Neoadjuvant chemotherapy has become an established part of treatment of stage II and III breast cancer, and the indications for use of this modality are constantly expanding.[1] Use of neoadjuvant chemotherapy allows for assessment of response to cytotoxic drugs in vivo, which is not only clinically relevant but also critical in terms of research endeavors assessing chemoresistance and response.[2] In addition, shrinking tumors preoperatively can make some women good candidates for breast conservation therapy.[3,4]

Physical examination (PE), ultrasonography (US), and mammography have all been used to assess tumor size in breast cancer patients both before and after neoadjuvant chemotherapy.[5–18] The accuracy of these modalities has been evaluated by looking at the correlation with pathologic measurements performed on surgical specimens. Studies in patients with small tumors (median size no larger than 2 cm) who did not receive neoadjuvant chemotherapy have generally shown that US gives the most accurate estimates of pathologic tumor size.[12,15] The results in studies that looked at residual tumor size after neoadjuvant chemotherapy are much more heterogeneous, with one study showing uniformly high correlations for all 3 modalities,[5] some showing a high correlation for PE[7] or for US,[6] and one indicating that all modalities are only moderately accurate in predicting residual tumor size.[8] Many of these studies have relied on very small sample sizes, and some have neglected to report on variables that might affect the accuracy of the measurements (eg, histology, tumor size).

This retrospective study assessed the accuracy of measurements of residual tumor size in 189 breast cancer patients following neoadjuvant chemotherapy. The clinical question addressed was: If PE, US, or mammography is used to estimate the size of the residual tumor after neoadjuvant chemotherapy, how often would the estimate be wrong, and

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what would the magnitude of the error be? We found that, although correlations with pathologic size were statistically significant for all 3 modalities, the level of correlation was only moderate; therefore, surgeons should interpret preoperative tumor size measurements with caution.

METHODS

This study was approved by the University of Texas M.D. Anderson Cancer Center Institutional Review Board. The initial patient population for the study consisted of 292 patients with invasive breast cancer who were enrolled in neoadjuvant chemotherapy protocols involving paclitaxel, FAC (fluorouracil, adriamycin, cyclophosphamide), or paclitaxel and FAC. All patients received 8 cycles of chemotherapy and underwent surgical resection of their tumors following the completion of chemotherapy. Forty patients had previously undergone an excisional biopsy for diagnosis and were excluded from the study. Of the remaining patients, 189 had postneoadjuvant therapy clinical tumor size assessments no more than 60 days prior to definite surgery. (This time frame was chosen as the best compromise to optimize the correlation between clinical measurements and pathologic findings, while maximizing the number of patients eligible for the study.) These 189 patients formed the population of interest for this study.

A retrospective chart review of the patients was undertaken. In addition to patient demographics, the largest unidimensional preoperative tumor size measurements (PE, US, mammography) before and after neoadjuvant therapy was recorded. Although some patients were referrals from other institutions, all pretreatment tumor size measurements were verified at M.D. Anderson prior to enrollment into a clinical protocol. The pathologic tumor size at the time of surgical resection was also noted. Pathologic size was initially determined on gross examination of the surgical specimen and then confirmed histologically on formalin-fixed tissue from serial sections made along the main axis of the tumor. In cases with mixed invasive ductal carcinoma and ductal carcinoma in situ (IDC/DCIS), both components were included in the measurement. In patients who received neoadjuvant chemotherapy, the site of the original tumor was marked with a metal clip prior to therapy. After therapy, for patients who had no grossly identifiable residual tumor at surgery, the marked location of the previous tumor was sectioned (5–10 sections) and examined for microscopic residual disease. If the clip was associated with fibrosis or a mass, the entire area of the abnormality was sectioned and examined. Pathologic complete response (pCR) was defined as total absence of cancer, including both invasive and in situ disease. In cases where scattered foci of residual disease were found within an area of abnormality, the total area of the scattered foci was estimated.

Other tumor features, including tumor grade, histologic subtype, estrogen/progesterone receptor status, and presence of lymphovascular invasion, were also recorded. Presence of EIC (extensive intraductal component, defined as >25% DCIS and the presence of DCIS away from the invasive tumor) was not available from the pathology reports, which generally did not estimate percentage of DCIS in a mixed lesion.

Spearman rank correlation analysis was used in 2 ways: 1) to measure the associations among PE, US, and mammography both before and after neoadjuvant chemotherapy, and 2) to measure the relationship between the preoperative clinical tumor measurements after neoadjuvant chemotherapy and the residual pathologic tumor size. Clinical and pathologic measurements were also compared categorically using the weighted kappa statistic. A kappa value of over 0.75 indicates excellent agreement, values between 0.4 and 0.74 represent fair to good reliability, and values below 0.4 represent poor reliability.[19]

RESULTS

Patient and Tumor Characteristics

The median patient age was 49.8 years (range, 28–75 years). The majority of patients (71.4%) were white, with 14.3% Hispanic, 8.5% black, and the remainder of various other ethnicities (Table 1).

The median pretreatment tumor size by clinical measurement ranged from 2.2 cm (range, 0.6–4.6 cm) by US to

TABLE 1. Patient and Tumor Characteristics

Feature	Value
Age (yr) [median (range)]	49.8 (28–75)
Ethnicity [no. (%) of patients]	
White	135 (71.4)
Black	16 (8.5)
Hispanic	27 (14.3)
Asian	6 (3.2)
Middle Eastern	4 (2.1)
Unknown	1 (0.5)
Pretherapy tumor size (cm) [median (range)]	
Physical examination (n = 177)	3.0 (0.0–6.0)
Mammography (n = 164)	2.5 (0.0–10.0)
Ultrasound (n = 187)	2.2 (0.6–4.6)
Pathological tumor size (median, range)	1.1 (0.0–8.0)
Histologic subtype [no. (%)]	
Infiltrating ductal carcinoma	173 (91.5)
Infiltrating lobular carcinoma	11 (5.8)
Other	5 (2.7)
Grade [no. (%)]	
1	14 (7.4)
2	79 (41.8)
3	95 (50.3)
Unknown	1 (0.5)
Estrogen receptor status [no. (%)]	
Positive	112 (59.3)
Negative	66 (34.9)
Unknown	11 (5.8)
Progesterone receptor status [no. (%)]	
Positive	97 (51.3)
Negative	72 (38.1)
Unknown	20 (10.6)
Lymphovascular invasion [no. (%)]	
Absent	64 (33.9)
Present	19 (10.0)
Unknown	106 (56.1)

TABLE 2. Correlation of Tumor Measurements

Comparison	Correlation Between Measurements*	
	Preneoadjuvant Chemotherapy	Postneoadjuvant Chemotherapy
PE vs. US	0.45	0.28
PE vs. M	0.40	0.26
US vs. M	0.58	0.35
PE vs. pathology	—	0.42
US vs. pathology	—	0.42
M vs. pathology	—	0.41

*Spearman rank correlation coefficients.
PE indicates physical examination; US, ultrasonography; M, mammography.

3.0 cm (range, 0.0–6.0 cm) by PE. More than 90% of patients had moderate to high grade infiltrating ductal carcinoma. Slightly more than half were estrogen receptor positive (59.3%) and progesterone receptor positive (51.3%). Lymphovascular invasion was noted in 23% (19 of 83) of patients for whom this characteristic was recorded.

Comparison of Tumor Size Measurements

All patients had clinical tumor size measurements by at least one modality (PE, US, mammography) no more than 60 days prior to surgical excision as per the inclusion criteria. Specifically, 132 patients had tumor size estimations prior to surgery using all 3 modalities, 21 patients had tumor size estimations by US and mammography only, 34 by PE and US only, and 11 by PE and mammography only. We examined the correlations among tumor size estimations by PE, US, and mammography both before and after neoadjuvant chemotherapy (Table 2). For all 3 comparisons (PE versus US, PE versus mammography, US versus mammography), there was a striking decrease in correlation for post-therapy measurements compared with pretherapy measurements. For example, the correlation between PE measurements and US measurements decreased from 0.45 to 0.28, with similar decreases for the other 2 comparisons.

We also examined the correlation between post-therapy clinical measurements and pathologic size and found correlation coefficients of 0.42, 0.42, and 0.41 for PE versus pathology, US versus pathology, and mammography versus pathology, respectively.

Accuracy of Clinical Measurements

Two approaches were used to assess the accuracy of PE, US, and mammography in predicting residual pathologic tumor size. First, scatterplots were constructed to provide a

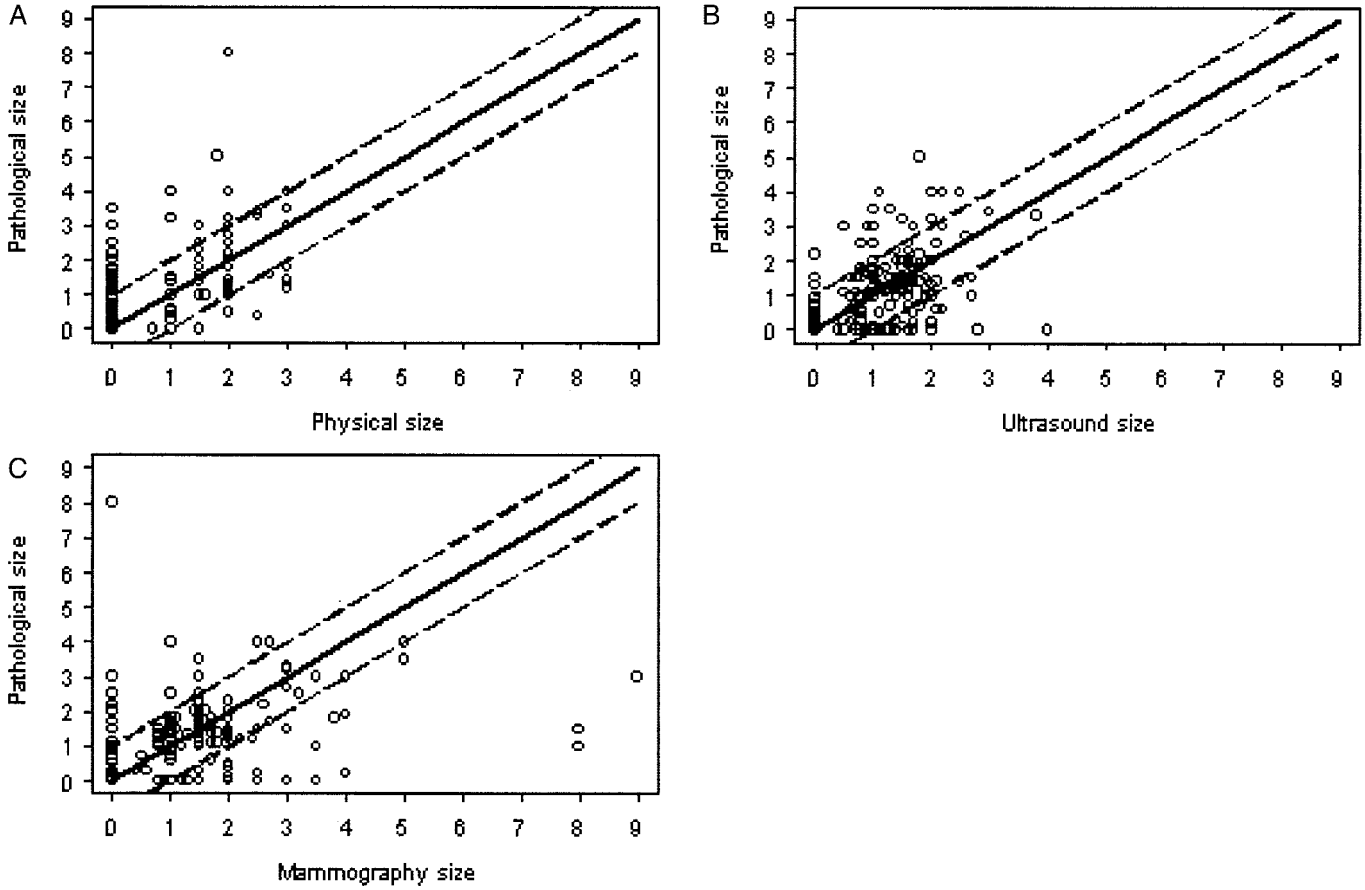

FIGURE 1. Scatterplots of pathologic tumor size versus tumor size estimations by (A) physical examination, (B) ultrasonography, and (C) mammography following neoadjuvant chemotherapy. Solid line indicates complete agreement between clinical tumor size estimate and residual pathologic tumor size. Dashed lines indicate agreement within ±1 cm.

TABLE 3. Categorical Assessment of Postneoadjuvant Chemotherapy: Clinical and Pathologic Measurements

Clinical Measurements (cm)	Pathologic Measurements (cm)				Weighted Kappa*
	0	0.1–1.0	1.1–2.0	>2.0	
Physical examination					
0	35†	30	36	7	0.24
0.1–1.0	4	5†	3	2	
1.1–2.0	1	8	14†	12	
>2.0	0	1	4	5†	
Ultrasonography					
0	14†	10	3	1	0.30
0.1–1.0	12	19†	16	6	
1.1–2.0	11	15	42†	12	
>2.0	3	3	3	7†	
Mammography					
0	19†	15	5	4	0.35
0.1–1.0	6	9†	12	2	
1.1–2.0	6	10	31†	6	
>2.0	4	4	9	12†	

*The weighted kappa statistic provides an indication of agreement between two measurement approaches with observations classified into one of several categories. It has a maximum value of 1 when agreement is perfect, and a value of zero when the agreement is no better than chance. Negative values show worse than chance agreement. A kappa value of > 0.75 represents excellent agreement, between 0.4 and 0.74 represents fair to good agreement, and below 0.4 represents poor agreement.

†Cases on the diagonal represent close agreement between clinical and pathologic measurements.

visual assessment (Fig. 1). In these plots, the solid line represents perfect accuracy, and the dashed lines represent accuracy within ±1 cm. PE was accurate to within ±1 cm in 66% of cases, US was accurate to within ±1 cm in 75% of cases, and mammography was accurate to within ±1 cm in 70% of cases. For measurement differences greater than 1 cm, PE underestimated pathologic size in 19 cases and overestimated in 5, US underestimated in 18 cases and overestimated in 14, and mammography underestimated in 13 cases and overestimated in 19.

Measurements from PE, US, and mammography were also compared with the residual pathologic tumor size using discrete categories: 0 cm, 0.1 to 1.0 cm, 1.1 to 2.0 cm, and >2.0 cm. The results of this cross-tabulation are shown in Table 3. Cases on the diagonals (†) represent close agreement between measurements. The preoperative clinical size estimates and the residual pathologic tumor size were compared using the weighted kappa statistic. Kappa values (0.24–0.35) indicated poor agreement between clinical measurements and pathologic measurement.

An examination of Table 3 indicates that clinical measurements resulted in a large number of false positives and false negatives. False positives occurred in patients who had measurable tumor by clinical assessment after neoadjuvant chemotherapy, but had no detectable tumor on pathologic examination. False-positive rates are calculated as the number of false positives divided by the total number of patients with no residual pathologic disease (ie, number of measured negatives + number of false positives). False negatives occurred in patients who had no measurable tumor by clinical assessment after neoadjuvant chemotherapy but had residual disease at the time of pathologic assessment. False negative rates are calculated as the number of false negatives divided by the total number of patients with some evidence of residual pathologic disease (number of measured positives + number of false negatives). As seen in Table 4, US resulted in the highest rate of false positives (65%) while physical examination showed the highest rate of false negatives (57%).

Influence of Tumor Characteristics on Tumor Size Estimation

It has been hypothesized that various histologic subtypes, such as invasive lobular carcinoma (ILC), may make preoperative tumor size estimation more difficult, particularly with US.[18] In this study, more than 90% of patients had invasive ductal carcinomas (IDC), 11 (5.8%) had ILC, and 5 (2.7%) had other histologic subtypes. Given the small

TABLE 4. False Negatives and False Positives in Postneoadjuvant Chemotherapy: Clinical Assessment of Tumor Size

Clinical Measurement	False Positive Rate (%)	False Negative Rate (%)
Physical examination	20% (5/40)	57% (73/127)
Ultrasound	65% (26/40)	10% (14/137)
Mammography	46% (16/35)	20% (24/119)

False positive rate = no. of false positive measurements divided by total number of negative measurements (ie, the number of measured negatives + the number of false positives); false negative rate = no. of false negative measurements divided by total number of positive measurements (ie, the number of measured positives + the number of false negatives).

number of patients with ILC in this study, it is difficult to estimate the accuracy of preoperative tumor size assessment in this group. To qualitatively assess whether ILC and other histologic subsets may have affected the accuracy of preoperative tumor size estimates, correlation coefficients were computed between clinical and pathologic measurements using the subset of 173 patients with IDC alone. In this subset, the correlation coefficients for tumor size estimation by PE, US, and mammography compared with residual pathologic tumor size (0.42, 0.45, and 0.36, respectively) corresponded fairly closely with those obtained in the total group (0.42, 0.42, and 0.41), suggesting at least that ILC and other histologic subtypes were not extreme outliers in this data set.

In addition, it has been proposed that tumor grade may impact the accuracy of preoperative tumor size assessment.[14] In our study, the correlation coefficients of tumor size estimation by US and mammography compared with residual pathologic tumor size in the group with low to intermediate grade tumors (0.40 and 0.46, respectively) were slightly higher than in the group with high grade tumors alone (0.36 and 0.40, respectively), but both were similar to the overall group. For PE, on the other hand, the correlation coefficient was substantially lower in low- to intermediate-grade tumors (0.26) compared with high-grade tumors (0.39).

DISCUSSION

Accurate clinical assessment of breast tumor size is a critical element in planning, monitoring, and assessing treatment strategies. The initial assessment of tumor size is used to select those patients who may benefit from neoadjuvant chemotherapy. Tumor size continues to be monitored to ensure that the selected drug regimen is having the desired effect, and ultimately to determine if the patient is a good candidate for breast-conserving surgery. Clinical assessment of tumor size and location, usually by US, also facilitates minimally invasive ablative procedures, including cryosurgery and radiofrequency ablation.

Clinical Measurements in Patients Who Received Neoadjuvant Chemotherapy

In this study, we examined the accuracy of clinical methods of tumor size assessment (PE, US, mammography) in comparison with direct measurement of the pathologic specimen in patients who received neoadjuvant chemotherapy. Overall, the agreement between clinical and pathologic measurement was only fair, with correlation coefficients slightly over 0.4 for all modalities. While these *r* values are statistically significant, this significance indicates only that there is an association between a clinical measurement and a pathologic measurement. Indeed, it would be surprising if there were not such an association, since the same physical object is being measured. This does not indicate, however, that the clinical size estimates are accurate predictors of pathologic size. To yield a prediction that is even 50% better than a random guess, the correlation must be at least 0.86.[20]

Although the majority of clinical measurements (66%–75%) were within 1 cm of pathologic measurements, this is not an inconsequential difference when dealing with residual tumors that, on average, were less than 2 cm in diameter. This level of inaccuracy could be critical when assessing patient suitability for breast conservation, or in determining whether a patient needs to be switched to an alternative drug regimen. In addition, 14% to 20% of clinical size estimates were more than 1 cm larger or smaller than pathologic size, and false-negative and false-positive rates were common. For example, numerous patients who had no residual tumor identified by pathology showed tumors 1 cm to 4 cm in diameter by US examination (Fig. 1).

We compared our findings with those in 5 previously published studies that assessed the accuracy of clinical measurement in patients who received neoadjuvant chemotherapy (Table 5).[5–9] Although one is immediately struck by the heterogeneity of results among these studies, an interesting observation can be made. There are basically 2 groups of studies: one group in which the data have been logarithmically transformed and analyzed with parametric statistics,[5,6] and one group in which the raw data have been analyzed using nonparametric statistics.[7–9] The studies in which the data were transformed showed a very high agreement between US measurements and pathologic measurements (r = 0.92 and 0.85, respectively), while the studies in which the raw data were analyzed showed moderate to poor *r* values of 0.60, 0.58, and 0.29. Transformation (logarithmic, exponential, etc). is a common statistical practice used to normalize

TABLE 5. Correlation Between Pathologic Tumor Size and Presurgical Tumor Size Estimated by Physical Examination or Imaging in Patients Treated With Neoadjuvant Chemotherapy

		Correlation Coefficient		
Reference (year)	**n**	**Physical Examination**	**Ultrasonography**	**Mammography**
Forouhi et al[5] (1994)*	35	0.88	0.96	0.94
Gawne-Caine et al[6] (1995)*	16	0.74	0.85	0.61
Herrada et al[7] (1997)†	100	0.73	0.60	0.65
Akashi-Tanaka et al[8] (2001)†	57	0.57	0.56	0.55
Fiorentino et al[9] (2001)†	141	0.68	0.29	0.33
Current series†	189	0.42	0.42	0.41

*Data were logarithmically transformed prior to calculation of Pearson's coefficient of correlation.
†Raw data were used for calculation of Spearman's rank correlation.

data, but the biologic interpretation of such a transformation is open to question. A high correlation coefficient between 2 sets of transformed data says only that the transformed data are correlated, not that the original data are. The correlation coefficients in original versus transformed data may be substantially different, and the determination of which is correct is not obvious. For example, we logarithmically transformed the data presented for US versus pathologic size in the study by Akashi-Tanaka et al.[8] The original analysis of the raw data yielded a correlation coefficient of 0.56 for the comparison of US size versus pathologic size. After transformation, the correlation dropped to 0.37. A similar manipulation of the US/pathology data originally presented in the study by Fornage et al[10] yielded a slight increase in correlation, from 0.84 in the raw data to 0.86 in the transformed data. Thus, the process of logarithmically transforming data can not be expected to yield predictable changes in the correlation between data sets.

Clinical Measurements in Patients Without Neoadjuvant Chemotherapy

Are clinical methods of assessing breast cancer size more accurate in patients who have not received neoadjuvant chemotherapy? While the present study was not designed to address this question, we did note that the internal agreement among PE, US, and mammography decreased substantially when postchemotherapy measurements were compared with prechemotherapy measurements. This suggests that the chemotherapy treatment itself may render the measurements less accurate. For example, as suggested in a small study by Nakamura et al,[21] chemotherapy may induce inflammatory or fibrotic changes in the tumor that make it less likely to image accurately or to be assessed accurately on physical examination.

A review of 9 published papers suggests that clinical approaches for measuring tumor size, especially ultrasonography, may be reasonably accurate in selected patients who do not receive neoadjuvant chemotherapy (Table 6).[10–18] The studies of Davis et al[12] and Hieken et al[15] found that the correlation between US size and pathologic size increased if the study population was restricted to patients with small tumors (T1, T2). The study by Hieken et al[15] found a higher standard error in patients with an EIC, and a study by Tressara et al[14] found a significant increase in the correlation between US and pathology when patients with EIC were removed from the sample. Pritt et al[18] examined the correlation between US and pathology in patients with IDC, ILC, or mixed IDC/ILC. While the correlation coefficients obtained for pure IDC or pure ILC were similar (0.82 and 0.81, respectively), the regression lines for these 2 comparisons were significantly different. This suggests that if the 2 histologic types were combined in one population, correlation coefficients would decrease significantly.

The study by Golshan et al[17] recorded the lowest correlation between US and pathology (r = 0.48). This study included 21% of patients with EIC, and this may partially explain the low correlation coefficient. In addition, 28% of patients in their study population had tumors identified as either ILC or mixed IDC/ILC.

Some of these studies were quite small, and conclusions from them should be approached with caution, as outlier values can strongly influence correlation coefficients

TABLE 6. Correlation Between Pathologic Tumor Size and Preoperative Tumor Size Estimated by Physical Examination or Imaging in Patients Not Treated With Neoadjuvant Chemotherapy

		Spearman Rank Correlation Coefficient		
Reference (year)	**n**	**Physical Examination**	**Ultrasonography**	**Mammography**
Fornage et al[10] (1987)	31	0.79	0.84	0.72
Madjar et al[11] (1993)	100	0.77	0.91	0.79
Davis et al[12] (1996)	12	NS	0.45	0.46
			0.88*	
Yang et al[13] (1997)	38	NS	0.93	0.84
Tressera et al[14] (1999)	174	NS	0.72	NS
Hieken et al[15] (2001)	146	NS	0.63†	0.40†
			0.72‡	0.49‡
Bosch et al[16] (2003)	73	0.42	0.68	0.44
Golshan et al[17] (2004)	202	NS	0.48§	0.66§
Pritt et al[18] (2004)				
IDC	129	NS	0.82	NS
ILC	41		0.81	
IDC/ILC	40		0.67	

*Increased correlation seen when tumors >3 cm and one tumor with post-chemotherapy fibrotic changes were eliminated.

†Lower standard error when tumors with an extensive intraductal component are eliminated.

‡T1/2 tumors only.

§This patient sample had a high percentage of patients with invasive lobular carcinoma (19% ILC and 10% mixed ILC/IDC) and a high percentage (25%) with an extensive intraductal component.

NS indicates not specified; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma.

in small samples. Nonetheless, these observations conservatively suggest that US can provide accurate predictions of pathologic tumor size in patient with small invasive ductal carcinomas that are EIC-negative, provided the patients do not receive neoadjuvant chemotherapy.

These provisional recommendations will be important in the selection of patients who may be candidates for minimally invasive ablation techniques, including cryotherapy and radiofrequency ablation. These techniques are critically dependent upon accurate imaging techniques. For example, the physics of heat transfer limits the size of a tumor that can be completely ablated by radiofrequency ablation, and protocols may be limited to patients with tumors no larger than 1.5 cm in diameter.[22] In the current study, 7 patients with US-imaged tumor sizes of 1.5 cm or less had pathologic tumor sizes of at least 3 cm. For future trials of these minimally invasive techniques, patients should be carefully selected to optimize the accuracy of available imaging techniques.

Other Approaches for Predicting Residual Tumor Size

Recently, other imaging modalities have been investigated to determine their accuracy at predicting residual pathologic tumor volume in patients with breast cancer treated with neoadjuvant chemotherapy. Contrast-enhanced computed tomography was shown in one study to be more accurate than physical examination or other conventional imaging techniques.[8] Magnetic resonance imaging (MRI) has become increasingly popular in breast imaging, and several studies have demonstrated a high correlation between tumor size as measured by MRI and pathologic tumor volume after neoadjuvant chemotherapy.[23–25] However, a recent study by Denis et al found that MRI may significantly underestimate residual disease in those patients who are treated with a taxane-containing regimen.[26]

New approaches for imaging breast tumors are being tested that are based on the function, metabolism, and molecular activity of tumor cells. An example of this is positron emission tomography (PET), which produces images based on metabolic and physiologic functions occurring in living cells. A downside to using PET as a stand-alone technology is the lack of anatomic landmarks seen on PET scans. When used in combination with CT scans, which offer high resolution anatomic imaging with appropriate contrast agents, the integrated scans combine the advantages of both technologies.[27] Another approach, in vivo cellular and molecular imaging, uses light wavelengths ranging from ultraviolet to near-infrared to quantify both biochemical and structural features of breast disease. This technique provides a noninvasive way to image and quantify vascularization. The synthesis of new light-absorbing and fluorescent probes sensitive to near-infrared irradiation will improve contrast and allow the detection of specific gene expression that may be modified during treatment with systemic therapy. These new techniques, which will be driven by research findings in molecular biology and nanobiotechnology, may one day provide precise estimates of tumor size, contributing to the goal of custom tailoring cancer treatment of individual patients.

CONCLUSION

Standard methods of clinically assessing tumor size (physical examination, ultrasonography, and mammography) are only moderately useful in patients who have received neoadjuvant chemotherapy. These patients can still be considered for breast-conserving surgery, but with the understanding that wider margins may be necessary. However, new minimally invasive ablation techniques such as cryosurgery and radiofrequency ablation require precise estimates of tumor size, and thus should be recommended only for selected patients. Typical inclusion characteristics for such procedures include the following: patient has not received neoadjuvant chemotherapy; small tumor size (<2 cm); confirmed diagnosis of IDC (no ILC or mixed IDC/ILC); no evidence of EIC; lesion is not close to chest wall or skin; and lesion can be well visualized on ultrasound. The inclusion of a wider range of patients in protocols to test these new minimally invasive techniques must await the development of more accurate imaging technology.

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